

# PATENT COOPERATION TREATY

PCT

## NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

From the INTERNATIONAL BUREAU

To:

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| Date of mailing (day/month/year)<br><b>14 December 1999 (14.12.99)</b>      |   |
| Applicant's or agent's file reference<br><b>7419/PC/2-ME</b>                | <b>IMPORTANT NOTIFICATION</b>   |
| International application No.<br><b>PCT/AU99/00914</b>                      | International filing date (day/month/year)<br><b>21 October 1999 (21.10.99)</b> |
| International publication date (day/month/year)<br><b>Not yet published</b> | Priority date (day/month/year)<br><b>21 October 1998 (21.10.98)</b>             |
| Applicant<br><b>THE UNIVERSITY OF QUEENSLAND et al</b>                      |   |

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
3. An asterisk(\*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
4. The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

| <u>Priority date</u>    | <u>Priority application No.</u> | <u>Country or regional Office<br/>or PCT receiving Office</u> | <u>Date of receipt<br/>of priority document</u> |
|-------------------------|---------------------------------|---|---|
| 21 Octo 1998 (21.10.98) | PP 6606                         | AU  | 08 Dece 1999 (08.12.99)                         |

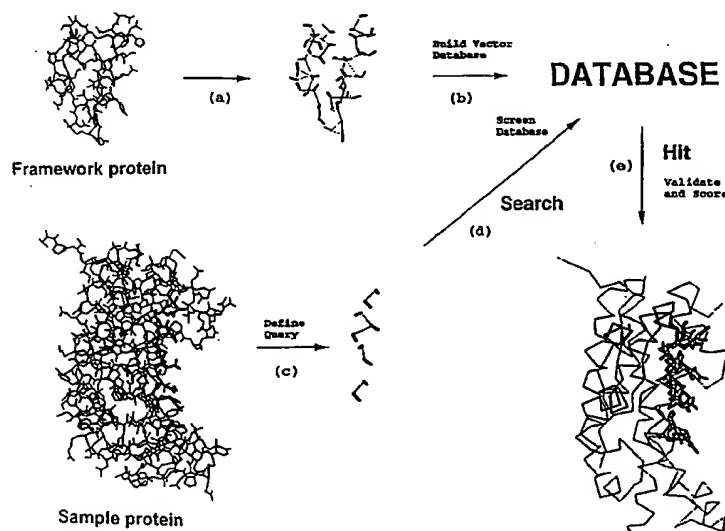
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| <p style="text-align: center;">The International Bureau of WIPO<br/>34, chemin des Colombettes<br/>1211 Geneva 20, Switzerland</p> <p>Facsimile N . (41-22) 740.14.35</p> | <p>Authorized officer</p> <p style="text-align: right;">Taïeb Akremi <i>TA</i></p> <p>Telephone No. (41-22) 338.83.38</p> |
|---|---|



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

|   |  |    |  |
|---|--|----|--|
| (51) International Patent Classification <sup>6</sup> :<br><b>C07K 14/61, 14/54, 14/535, G06F 17/30</b>   |  | A1 | (11) International Publication Number:<br><b>WO 00/23474</b>   |
|   |  |    | (43) International Publication Date:<br>27 April 2000 (27.04.00)   |
| (21) International Application Number: PCT/AU99/00914<br>(22) International Filing Date: 21 October 1999 (21.10.99)<br>(30) Priority Data:<br>PP 6606                      21 October 1998 (21.10.98)                      AU<br>(71) Applicant (for all designated States except US): THE UNIVERSITY OF QUEENSLAND [AU/AU]; St. Lucia, Brisbane, QLD 4072 (AU).<br>(72) Inventors; and<br>(75) Inventors/Applicants (for US only): SMYTHE, Mark, Leslie [AU/AU]; 8 Morgan Terrace, Bardon, QLD 4065 (AU). DOOLEY, Michael, John [AU/AU]; 5 Kewarra Street, Kenmore, QLD 4069 (AU). ANDREWS, Peter, Ronald [AU/AU]; 311 Swann Road, St. Lucia, QLD 4067 (AU).<br>(74) Agent: FISHER ADAMS KELLY; Level 13, AMP Place, 10 Eagle Street, Brisbane, QLD 4000 (AU). |  |    | (81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).<br><br>Published<br>With international search report. |

(54) Title: PROTEIN ENGINEERING



## (57) Abstract

A method of protein engineering is provided wherein a searchable computer database is created comprising entries in the form of descriptions of a location and orientation in 3D space of side chains of the constituent amino acid residues of a framework protein. A query is created which corresponds to a description of a location and orientation in 3D space of respective side chains of amino acid residues of a sample protein. The location and orientation in 3D space of constituent side-chains is preferably described as a  $C\alpha-C\beta$  vector. The query is used to search the database and thereby identify a hit which corresponds to a framework protein having structural similarity with said sample protein. Framework protein "hits" so identified may be suitable candidates for further modification. A particular advantage of the present invention is that a modified framework protein may display one or more desired characteristics, such as a function similar to or inhibitory of the sample protein.

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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**PATENT COOPERATION TREATY**  
**PCT**  
**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

(PCT Article 36 and Rule 70)

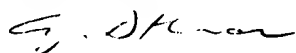
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| Applicant's or agent's file reference<br>2/7419/PC-MLE/JAB  | <b>FOR FURTHER ACTION</b>  | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416). |
| International application No.<br><b>PCT/AU99/00914</b>  | International filing date ( <i>day/month/year</i> )<br>21 October 1999 | Priority Date ( <i>day/month/year</i> )<br>21 October 1998   |
| International Patent Classification (IPC) or national classification and IPC<br><br><b>Int. Cl. <sup>7</sup> C07K 14/61, 14/54, 14/535 G06F 17/30</b> |  |  |
| Applicant<br><b>THE UNIVERSITY OF QUEENSLAND et al</b>  |  |  |

|    |   |
|----|---|
| 1. | This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.  |
| 2. | This REPORT consists of a total of 5 sheets, including this cover sheet.<br><br><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).<br><br>These annexes consist of a total of 12 sheet(s).   |
| 3. | This report contains indications relating to the following items:<br><br>I <input checked="" type="checkbox"/> Basis of the report<br>II <input type="checkbox"/> Priority<br>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability<br>IV <input checked="" type="checkbox"/> Lack of unity of invention<br>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement<br>VI <input checked="" type="checkbox"/> Certain documents cited<br>VII <input type="checkbox"/> Certain defects in the international application<br>VIII <input type="checkbox"/> Certain observations on the international application |

|   |  |
|---|--|
| Date of submission of the demand<br>2 March 2000  | Date of completion of the report<br>13 July 2000   |
| Name and mailing address of the IPEA/AU<br>AUSTRALIAN PATENT OFFICE<br>PO BOX 200, WODEN ACT 2606, AUSTRALIA<br>E-mail address: pct@ipaaustralia.gov.au<br>Facsimile No. (02) 6285 3929 | Authorised Officer<br><br><b>G. D. HEARDER</b><br>Telephone No. (02) 6283 2553 |

**I. Basis of the report****1. With regard to the elements of the international application:\***

- ☐ the international application as originally filed.
- ☒ the description, pages 1-7, 15-60, as originally filed,  
pages , filed with the demand,  
pages 8-14, 14a, received on 6 June 2000 with the letter of 6 June 2000
- ☒ the claims, pages , as originally filed,  
pages , as amended (together with any statement) under Article 19,  
pages , filed with the demand,  
pages 61-64, received on 6 June 2000 with the letter of 6 June 2000
- ☒ the drawings, pages 1/14-14/14, as originally filed,  
pages , filed with the demand,  
pages , received on with the letter of
- ☐ the sequence listing part of the description:  
pages , as originally filed  
pages , filed with the demand  
pages , received on with the letter of

**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**

These elements were available or furnished to this Authority in the following language which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, was on the basis of the sequence listing:**

- ☒ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

**4. ☐ The amendments have resulted in the cancellation of:**

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/fig.

**5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\***

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report

**IV. Lack of unity of invention**

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:

The international application does not comply with the requirements of unity of invention because it does not relate to one invention or to a group of inventions so linked as to form a single general inventive concept. In coming to this conclusion this Authority has found that there are different inventions as follows:

1. Claims 1-19 are directed to a method of protein engineering by creating a computer database which has entries corresponding to descriptions of locations and orientations in 3D space of side chains of amino acids, and using a framework protein and sample protein, as well as a modified framework protein produced by that method. It is considered that said method of protein engineering and said protein produced by that method, comprise a first "special technical feature".
2. Claims 20-26 are directed to engineered proteins with particular characteristics, not necessarily engineered by the methods of claims 1-17. It is considered that said engineered proteins comprises a second "special technical feature".
3. Claims 27-30 are directed to a computer program for searching a protein database which has entries corresponding to distance matrix representations of  $C_{\alpha}$ - $C_{\beta}$  vectors. This protein database is not necessarily the same database used in claims 1-17. It is considered that said computer program comprises a third "special technical feature".

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

|                               |             |     |
|-------------------------------|-------------|-----|
| Novelty (N)                   | Claims 1-30 | YES |
|                               | Claims      | NO  |
| Inventive step (IS)           | Claims 1-30 | YES |
|                               | Claims      | NO  |
| Industrial applicability (IA) | Claims 1-30 | YES |
|                               | Claims      | NO  |

**2. Citations and explanations (Rule 70.7)**

No individual citation or obvious combination of citations disclose the features of claims 1-30.

See however the indication contained in Box VI "Certain Documents Cited".

**VI. Certain documents cited****1. Certain published documents (Rule 70.10)**

|      | Application No.<br>Patent No. | Publication date<br>(day/month/year) | Filing date<br>(day/month/year) | Priority date ( valid claim)<br>(day/month/year) |
|------|-------------------------------|--------------------------------------|---------------------------------|--|
| P, X | EP 936565 A1                  | 18 August 1999                       | 15 February 1999                | 16 February 1998                                 |
| P, X | WO 99/22019 A1                | 6 May 1999                           | 29 October 1998                 | 29 October 1997                                  |
| P, X | WO 99/18440 A1                | 15 April 1999                        | 2 October 1998                  | 2 October 1997                                   |
| P, X | WO 99/01409 A1                | 14 January 1999                      | 2 July 1998                     | 3 July 1997                                      |
| P, A | US 5878373 A                  | 2 March 1999                         | -                               | 6 December 1996                                  |

EP 936565 discloses a method of searching a database of three-dimensional protein structures; which appears to cover the features of claims 1-14, 16-19, 27 and 28.

WO 99/22019 discloses a method for determination of function of proteins or domains comprising determining 3 dimensional structure and comparing with known structures with known function in a protein data bank; which appears to include the features of claims 1-14, 16-19, 27 and 28.

WO 99/18440 discloses a method for inferring a three-dimensional structure of a protein; which appears to include the features of claims 1, 7-13, 16, 17, 27 and 28, (see Derwent Abstract).

WO 99/1409 discloses a method of inferring the biological function or activity of a protein whose three-dimensional configuration is know or can be inferred; which appears to include the features of claims 1, 7-13, 16, 17, 27 and 28, (see Derwent Abstract).

**2. Non-written disclosures (Rule 70.9)**

| Kind of non-written disclosure | Date of non-written disclosure<br>(day/month/year) | Date of written disclosure referring to<br>non-written disclosure<br>(day/month/year) |
|--------------------------------|--|---|
|--------------------------------|--|---|